REMARKS

1-6. Claims 1-14 are in the case. The claims have been made subject to a requirement to restrict. By a provisional election, made by phone on 1/3/06 claim 2 has been elected, drawn to a method for increasing the resistance of a host cell to aromatic carboxylic acids. Claims 3-13 are linking claims and will be examined in the present application. Applicants hereby affirm this election.

Claims 1 and 14 are withdrawn as drawn to a non-elected invention.

The election of claims has not altered inventorship.

All claims stand rejected under 35 USC § 112

Claims 2 – 5, 8, 9, 11, and have been amended to more clearly describe applicants' invention.

Claims 10 and 13 are canceled by this amendment

No new matter has been added.

Objections to the Specification

7. The title is objected to as not being descriptive. The title has been amended to overcome this objection.

8. Claims 3-13 are objected to for depending from a non-elected claim. The claims have been amended to overcome this objection.

Claim Rejections – 35 USC § 112, 2d paragraph

9-10. Claims 2-13 are rejected under 35 USC § 112, 2d paragraph of indefiniteness. Specifically the claims lack essential steps. The examiner suggests that the essential steps omitted are those of transforming and overexpressing the *yhcP* gene and the *yhcQ* gene in the host cell. The examiner points to MPEP 2172.01. Applicants respectfully traverse.

Applicants submit that transforming and overexpressing the *yhcP* gene and the *yhcQ* gene are not essential limitations of the present claims. The invention requires that the expression of *yhcP* and *yhcQ* be upregulated. Up regulation may be achieved by methods well known in the art that do not require transforming the host cell with the gene, particularly in situations where the gene is endogenous to the host cell. The discussion the specification beginning at page 16, line 13 outlines a number of methods whereby the genes in question may be upregulated that do not involve transformation. For example, placing the gene under the control of a strong promoter may be accomplished through targeted homologous recombination of the promoter without transforming the host with the gene. Additionally, random or site specific mutagenesis is a method well established in the art that may accomplish the same purpose.

MPEP 2164.08(c), cited in section 2172.01 suggest that a rejection under 35 USC § 112 for the omission of essential steps is improper in the face of broad language in the disclosure including that of the abstract.

> "Limiting an applicant to the preferred materials in the absence of limiting prior art would not serve the constitutional purpose of promoting the progress in the useful arts. Therefore, an enablement rejection based on the grounds that a disclosed critical limitation is missing from a claim should be made only when the language of the specification makes it clear that the limitation is critical for the invention to function as intended. Broad language in the disclosure, including the abstract, omitting an allegedly critical feature, tends to rebut the argument of criticality. " MPEP 2164.08(c)

Applicants submit that the claims as written are clear and omit no essential steps. In view of broader language in the specification applicants submit this rejection is improper and respectfully request it's withdrawal.

11. Claim 9 is rejected under 35 USC § 112, 2d paragraph for indefiniteness. Specifically, Claim 9 is indefinite with respect to the association of SEQ ID NO's and the *yhcQ* and *yhcP* genes. The claim has been amended to overcome this rejection.

12-13. Claims 2-8 and 11-13 are rejected under 35 USC § 112, 1st paragraph as failing to comply with the written description requirement. It is the examiner's view that the specification adequately describes only a *yhcQ* as defined by SEQ ID NO:2 and a *yhcP* as defined by SEQ ID NO:1, but does not describe genes of these functions beyond those defined by the specific SEQ ID NO's. The Examiner cites *California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997); and *Fiers v. Revel Co.*, 984 F.2d 1164 (Fed. Cir. 1993) in support of this rejection. Applicants respectfully traverse.

The Examiner asserts that the names *yhcQ* and *yhcP* define genus' of genes that have widely differing structural, chemical and physiochemical properties. The specification does not describe any structural features commonly possessed by these genes and thus the person of skill in the art cannot visualize the identity of the members of each genus for use in the claimed method.

Applicants submit that the specification describes the *yhcQ* and *yhcP* genes in sufficient detail that the person of skill in the art would recognize that the inventor was in possession of the invention at the time it was made. In particular, specific examples of these genes are given in SEQ ID NO:1 and 2 as noted by the Examiner. Alternate sources of analogous genes are given (see page 17, line 5-21). Descriptions on how to use the species described in the specification to find homologous versions of these genes (see page 18, the discussion beginning at line 12). In making his rejection Applicants submit that the Examiner

is suggesting that the specification fails the written description requirement because genes that are known in the art are not re-described in the specification.

In recently decided *Capon v. Eshhar*, (Fed. Cir., No. 03-1480, 8/12/05.), dealing with the question of the adequacy written description for genes not specifically described in the specification but cross referenced to the known literature, the Federal Circuit has held that there is no *per se* rule requiring recitation in the specification of the nucleotide sequence of claimed DNA when that sequence is already known in the field (*Capon* at page 20). In reference to *Lilly* and *Fiers* the court in *Capon* has stated:

> "[N]one of the cases to which the Board attributes the requirement of total DNA re-analysis, i.e., Regents v. Lilly, Fiers v. Revel, Amgen, or Enzo Biochem, require a re-description of what was already known. In Lilly, 119 F.3d at 1567, the cDNA for human insulin had never been characterized. Similarly in Fiers, 984 F.2d at 1171, much of the DNA sought to be claimed was of unknown structure, whereby this court viewed the breadth of the claims as embracing a "wish" or research "plan." [*Capon*, at page 14]

and concludes: "When the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh."[*Capon* at page 15]. The court goes on to note that the specifications under review both presented "...general teachings of how to select and recombine DNA..." and referenced examples of the specific genes and proteins of the claims in the literature. [*Capon* at page17-18]. This level of description was held to be sufficient by the court to meet written description.

Applicants submit that the present specification references specific examples of homologous genes to the specific *yhcQ* and *yhcP* genes claimed as well as general teachings on how to select these homologs (cited above), and that under *Capon* this description complies with the written description of 35 USC § 112 and under these facts is not controlled by *Lilly* and *Fiers*.

The claims are additionally rejected for not describing gene elements (promoters, regulatory elements etc..) which are essential to the function of the expression of the *yhcQ* and *yhcP* genes. Applicants traverse.

Claim 9 has been amended to remove the limitation of a "suitable promoter". Claim 10 has been canceled. Claim 12 has been amended to incorporate the limitations of claim 13 and now only recites specific promoters, well described in the specification (see discussion beginning on page 21, line 19). In view of these amendments to the claims Applicants submit that the promoters recited in the claims are all adequately described in the specification.

14. Claims 2-8 and 11-13 are rejected under 35 USC § 112, 1st paragraph for lack of enablement. The Examiner finds that the claims are enabled for a method for increasing the

resistance of a host cell to aromatic carboxylic acids involving the polynucleotides of SEQ ID NO:1 and 2 however are not enabled for any *yhcQ* and *yhcP* genes. The Examiner cites the *Wands* factors in support of his assertion. Applicants traverse.

The touchstone of enablement is whether the skilled person would be required to perform undue experimentation in order to practice the invention. Some experimentation is acceptable (MPEP 2164). The factors to be considered in determining if experimentation is "undue" were set forth in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). and include:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Applicants submit that in considering the *Wands* factors under the totality of the circumstances that the present invention is enabled for homologs of *E. coli yhcQ* and *yhcP* genes. It is noted here that Claim 2 ahs been amended to recite the limitation that the *yhcQ* and *yhcP* genes are derived from *E. coli*. Considering the *Wands* factors in this context the claims are not overly broad as they are limited to genes isolated from *E. coli* only, decreasing the burden for enablement. The nature of the invention is the upregualtion of the *yhcQ* and *yhcP* genes, which is common and well known in the art. The state of the art for up-regulation of genes is highly advanced and methods for up-regulation of genes is common and well known and fully described in the specification (see the discussion on page 21, beginning at line 19 for a description of suitable promoters for up-regulation; page 17 beginning at line 5 for a discussion of sources of *E. coli* homologs of the *yhcQ* and *yhcP* genes; page 18 beginning at line 12 for a discussion of methods of isolating homologs of the *yhcQ* and *yhcP* genes for up-regulation). The level of the skilled person in the art of gene regulation is high and aided by commercially available kits and tools and protocols (see Sambrook et al, cited on page 22, line 21). The inventor has provided explicit direction in the working examples and the specification, teaching methods for the up-regulation of the genes of the invention making the quantity of experimentation needed by the skilled person to make and use the invention low.

In view of the details provided in the specification and examples, Applicant's submit that the claims are enabled as amended and comply with 35 USC § 112, 1st paragraph.

In view of the foregoing reconsideration for the claims as amended and withdrawal of all rejections is respectfully requested.

Respectfully submitted,

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